Docket: 7214.07

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Charles N. Serhan		
Appln. No.:	Filed herewith		
Filed:	October 19, 2001	Previous Examiner:	Dwayne C. Jones
Title:	Regulation of Phospholipase D Activity	Previous Group Art Unit:	1614

PRELIMINARY AMENDMENT

Commissioner for Patents
BOX PATENT APPLICATION
Washington, D.C. 20231

Sir:

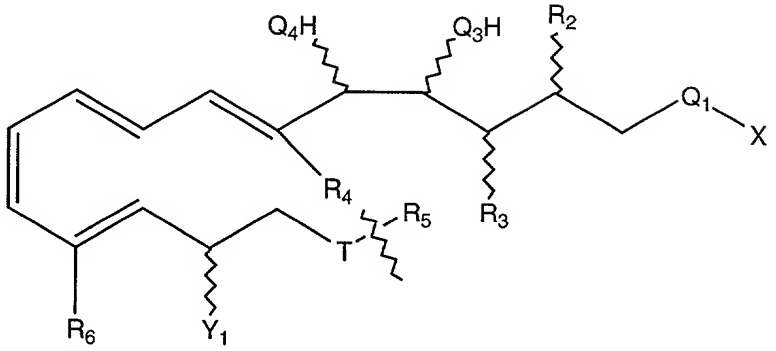
Please preliminarily amend the above-identified application as follows:

<u>In the specification</u>:

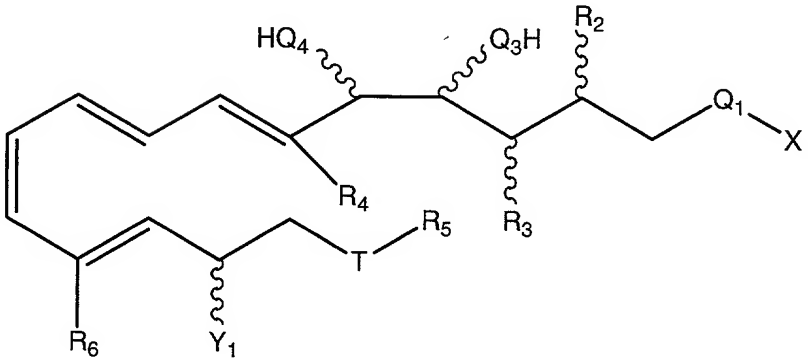
At page 1, lines 3 through 5, please delete the entire paragraph after "Cross-Reference to Related Applications" and replace with the following paragraph:

- - This application is a continuation application of U.S. Patent Application No. 09/525,157, filed March 14, 2000, which in turn claims priority to U.S. Provisional Patent Application No. 60/125,194, filed March 18, 1999, the contents of which are incorporated herein by reference. - -

At page 11, lines 5 through 10, please delete



and insert therefore - -



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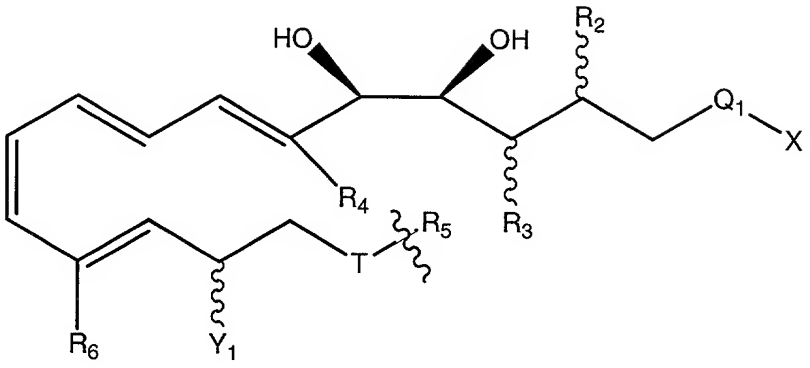
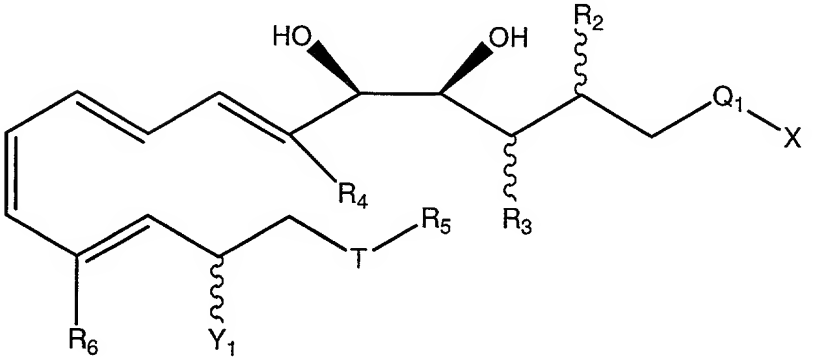
At page 14, lines 1 through 7, please delete



and insert therefore - -



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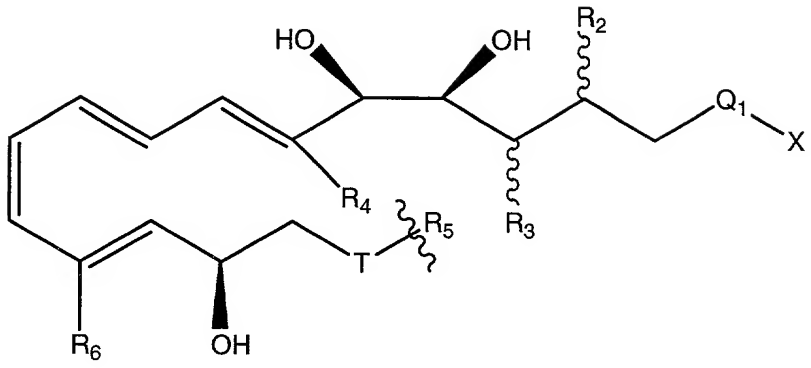
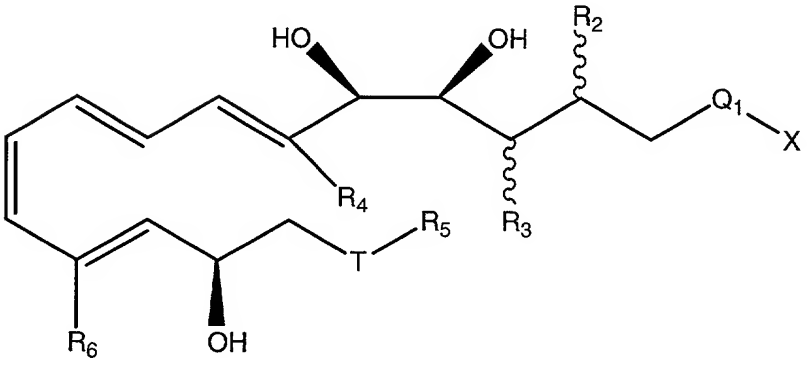
At page 17, lines 1 through 7, please delete



and insert therefore - -



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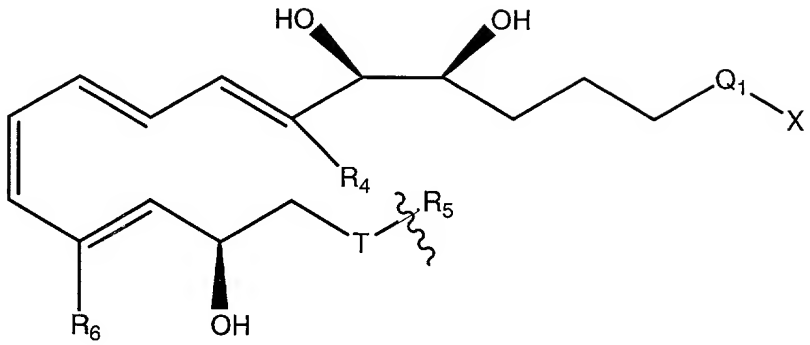
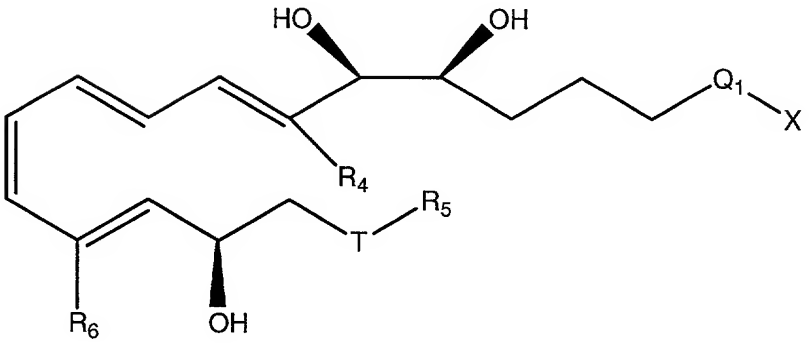
At page 19, lines 21 through 30, please delete



and insert therefore - -



- -

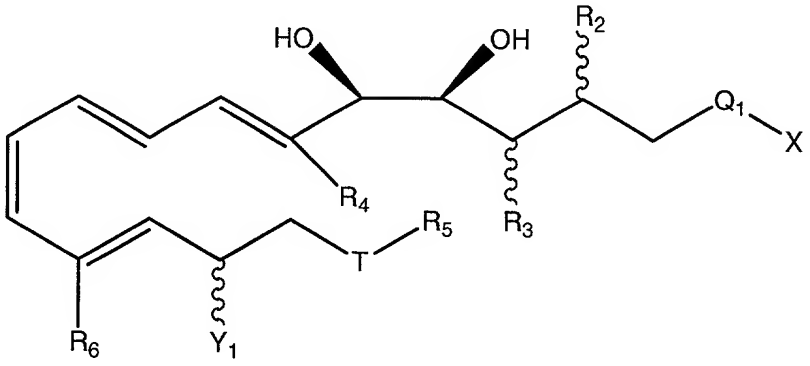
In the claims:

Please cancel claims 2 through 16 inclusive.

Please add new claims 17 through 32 as follows:

17. (New) A method for modulating a disease or condition associated with phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation in a subject, comprising

administering to the subject an effective anti-inflammatory amount of a lipoxin analog having the formula



wherein X is R_1, OR_1, or SR_1;

wherein R_1 is

(i) a hydrogen atom;

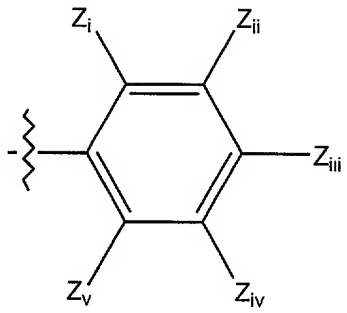
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;

(iii) a cycloalkyl of 3 to 10 carbon atoms;

(iv) an aralkyl of 7 to 12 carbon atoms;

(v) phenyl;

(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or

(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;

(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;

(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;

(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

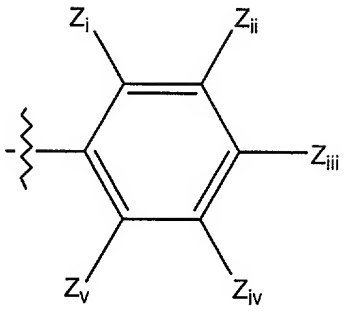
(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;

(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;

(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

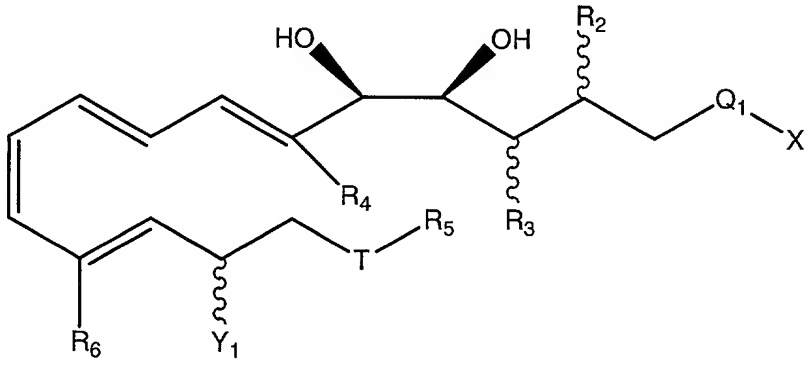
wherein T is O or S, and pharmaceutically acceptable salts thereof, such that a disease or condition associated with PLD initiated polymorphoneutrophil (PMN) inflammation in a subject is modulated.

18. (New) The method of claim 17, wherein said method is performed *in vitro*.

19. (New) The method of claim 17, wherein said method is performed *in vivo*.

20. (New) A method for treating phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation in a subject, comprising

administering to the subject an effective anti-inflammatory amount of a lipoxin analog having the formula



wherein X is R_1, OR_1, or SR_1;

wherein R_1 is

(i) a hydrogen atom;

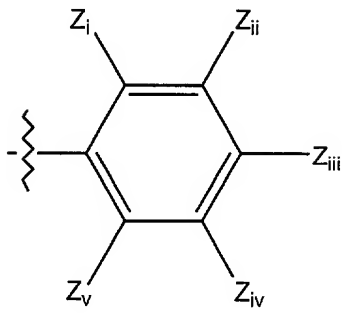
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;

(iii) a cycloalkyl of 3 to 10 carbon atoms;

(iv) an aralkyl of 7 to 12 carbon atoms;

(v) phenyl;

(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or

(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;

(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;

(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;

(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons

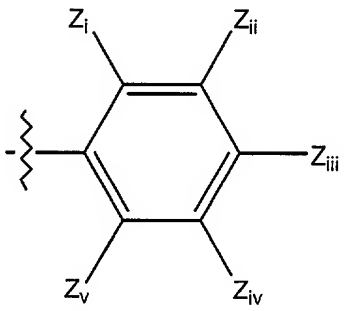
atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;

(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;

(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

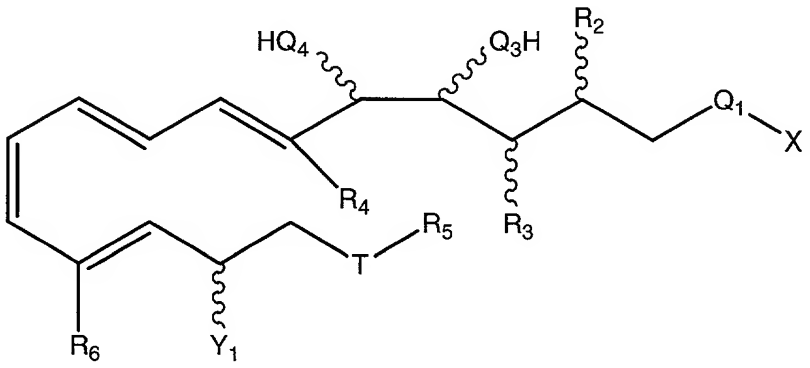
wherein T is O or S, and pharmaceutically acceptable salts thereof, such that PLD initiated polymorphoneutrophil (PMN) inflammation is treated in a subject.

21. (New) The method of claim 20, wherein said method is performed *in vitro*.

22. (New) The method of claim 20, wherein said method is performed *in vivo*.

23. (New) A method for modulating a disease or condition associated with phospholipase D (PLD) initiated superoxide generation or degranulation activity in a subject, comprising

administering to the subject an effective anti-PLD amount of a lipoxin analog having the formula



wherein X is R_1, OR_1, or SR_1;

wherein R_1 is

(i) a hydrogen atom;

(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight

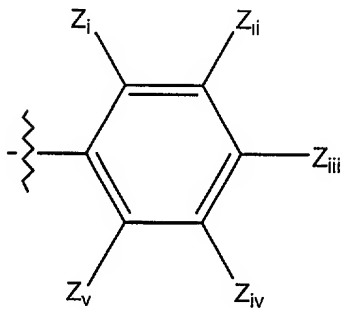
chain or branched;

(iii) a cycloalkyl of 3 to 10 carbon atoms;

(iv) an aralkyl of 7 to 12 carbon atoms;

(v) phenyl;

(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or

(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;

(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;

(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;

(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or

branched; or

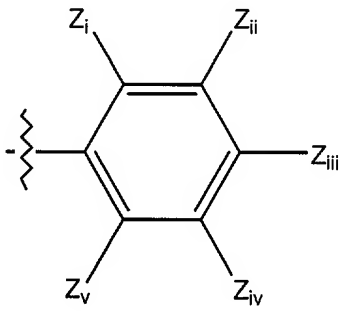
(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;

(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $–NO_2$, –CN, $–C(=O)–R_1$, $–SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, orCH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;

(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

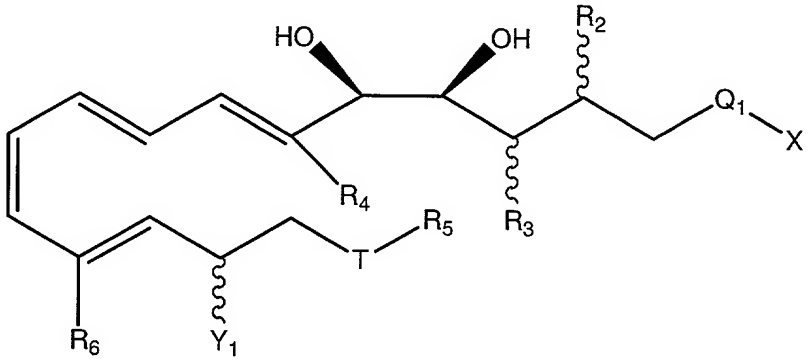
wherein T is O or S, and pharmaceutically acceptable salts thereof, such that a disease or condition associated with PLD initiated superoxide generation or degranulation activity in a subject is modulated.

24. (New) The method of claim 23, wherein said method is performed *in vitro*.

25. (New) The method of claim 23, wherein said method is performed *in vivo*.

26. (New) A method for treating phospholipase D (PLD) initiated superoxide generation or degranulation in a subject, comprising

administering to the subject an effective anti-PLD amount of a lipoxin analog having the formula



wherein X is R_1, OR_1, or SR_1;

wherein R_1 is

(i) a hydrogen atom;

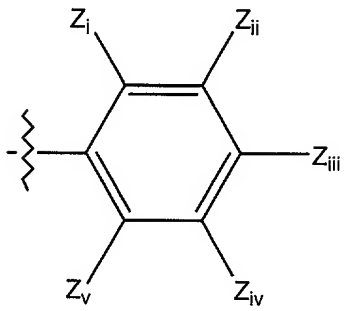
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;

(iii) a cycloalkyl of 3 to 10 carbon atoms;

(iv) an aralkyl of 7 to 12 carbon atoms;

(v) phenyl;

(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, –CN, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or

(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;

(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;

(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;

(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

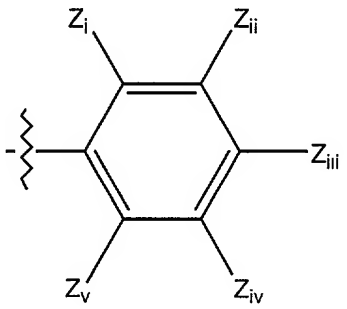
(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;

(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $–NO_2$, –CN, $–C(=O)–R_1$, $–SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or

branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;

(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

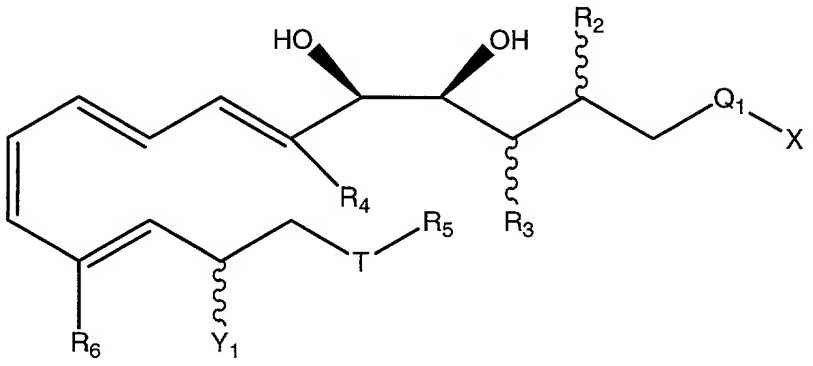
wherein T is O or S, and pharmaceutically acceptable salts thereof, such that PLD initiated superoxide generation or granulation is treated in a subject.

27. (New) The method of claim 26, wherein said method is performed *in vitro*.

28. (New) The method of claim 26, wherein said method is performed *in vivo*.

29. (New) A packaged pharmaceutical composition for treating a disease or condition associated with phospholipase D (PLD) initiated activity in a subject, comprising:

a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R_1, OR_1, or SR_1;

wherein R_1 is

(i) a hydrogen atom;

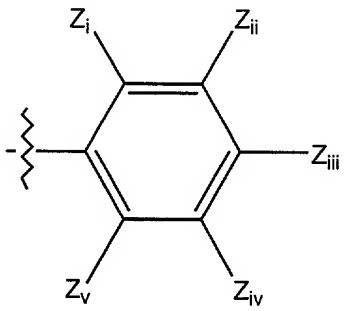
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;

(iii) a cycloalkyl of 3 to 10 carbon atoms;

(iv) an aralkyl of 7 to 12 carbon atoms;

(v) phenyl;

(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or

(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;

wherein Q_3 and Q_4 are each independently O, S or NH;

wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;

(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;

(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;

(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

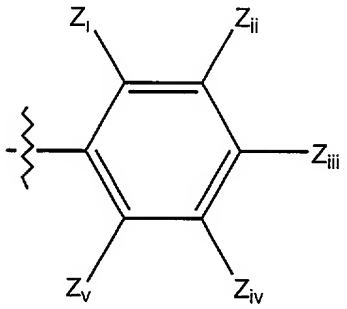
(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;

(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $–NO_2$, –CN, $–C(=O)–R_1$, $–SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;

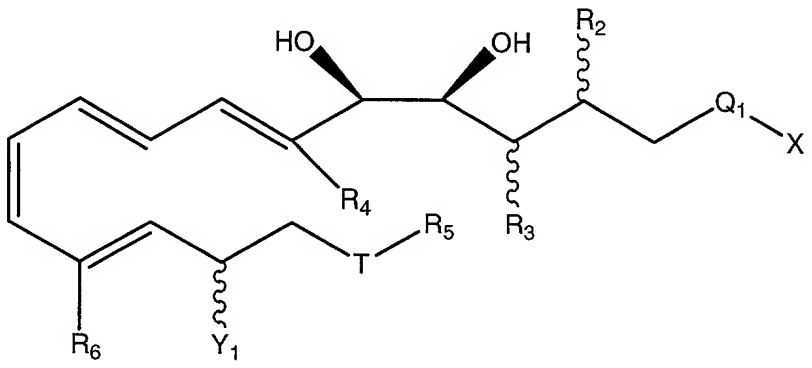
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein T is O or S, and pharmaceutically acceptable salts thereof; and

instructions for using said lipoxin compound for treating a disease or condition associated with PLD initiated activity in the subject.

30. (New) A packaged pharmaceutical composition for treating phospholipase D initiated activity in a subject, comprising:

a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R_1, OR_1, or SR_1;

wherein R_1 is

(i) a hydrogen atom;

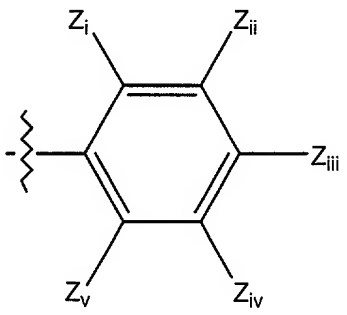
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;

(iii) a cycloalkyl of 3 to 10 carbon atoms;

(iv) an aralkyl of 7 to 12 carbon atoms;

(v) phenyl;

(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or

(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;

(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;

(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;

(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

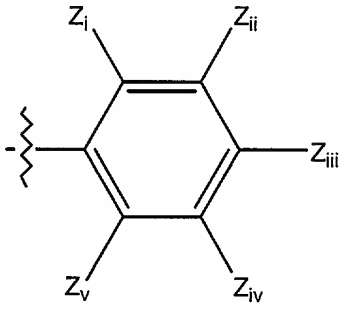
(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;

(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $–NO_2$, –CN, $–C(=O)–R_1$, $–SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;

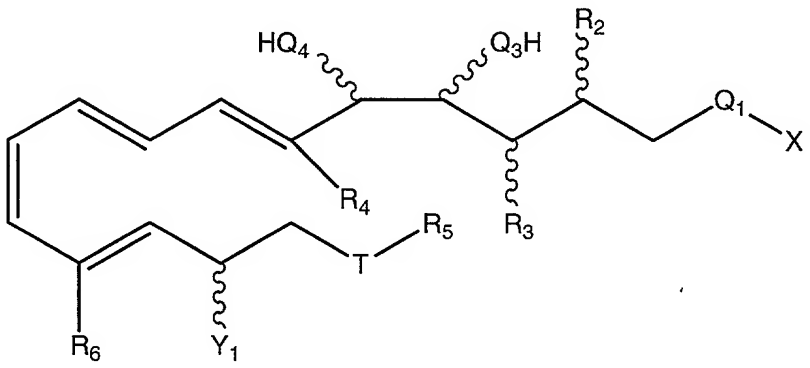
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein T is O or S, and pharmaceutically acceptable salts thereof; and

instructions for using said lipoxin compound for treating PLD initiated activity in the subject.

31. (New) A packaged pharmaceutical composition for treating a disease or condition associated with phospholipase D (PLD) initiated superoxide generation or degranulation activity in a subject, comprising:

a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R_1, OR_1, or SR_1;

wherein R_1 is

(i) a hydrogen atom;

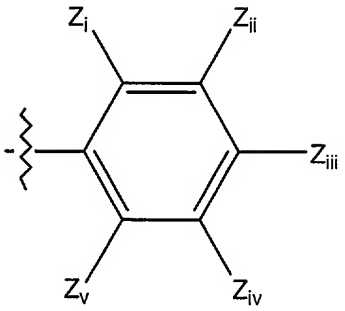
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;

(iii) a cycloalkyl of 3 to 10 carbon atoms;

(iv) an aralkyl of 7 to 12 carbon atoms;

(v) phenyl;

(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or

(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;

(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;

(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;

(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons

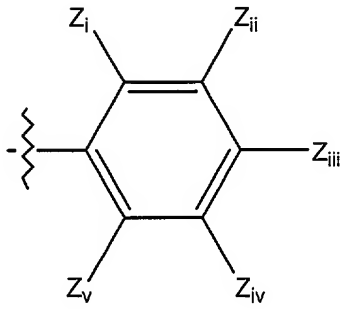
atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;

(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;

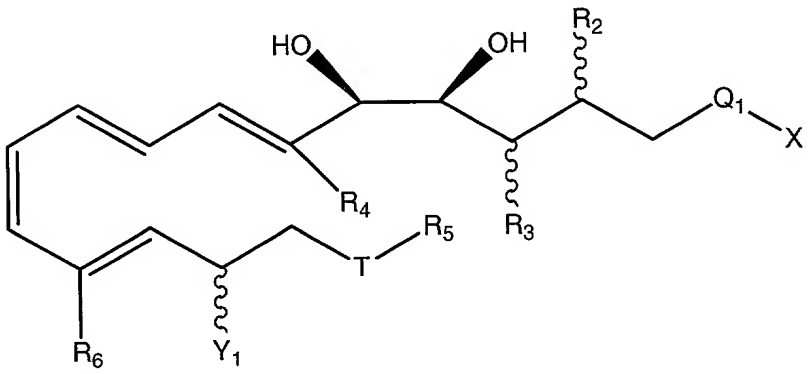
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein T is O or S, and pharmaceutically acceptable salts thereof; and

instructions for using said lipoxin compound for treating a disease or condition associated with PLD initiated superoxide generation or degranulation activity in the subject.

32. (New) A packaged pharmaceutical composition for treating phospholipase D (PLD) initiated superoxide generation or degranulation activity in a subject, comprising:

a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R_1, OR_1, or SR_1;

wherein R_1 is

(i) a hydrogen atom;

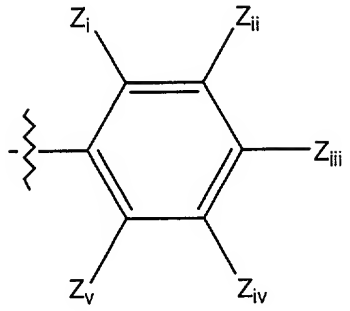
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;

(iii) a cycloalkyl of 3 to 10 carbon atoms;

(iv) an aralkyl of 7 to 12 carbon atoms;

(v) phenyl;

(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, –CN, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or

(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;

(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;

(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;

(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched,

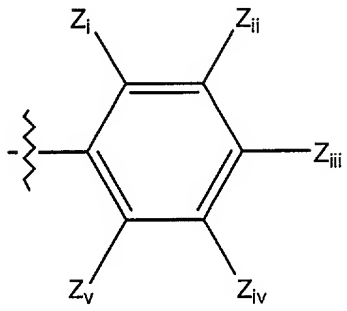
provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;

(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;

(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein T is O or S, and pharmaceutically acceptable salts thereof; and

instructions for using said lipoxin compound for treating PLD initiated superoxide generation or degranulation activity in the subject.

REMARKS

Claims 1 and 17 through 32 are pending.

The specification has been amended to correct for an obvious typographical errors on pages 11, 14, 17 and 19 and to more clearly define the invention.

Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached pages are captioned "Version with Markings to Show Changes Made."

Conclusion

In view of the foregoing, Applicant submits that all pending claims are allowable. The Examiner is invited to telephone the undersigned attorney for Applicants in the event that such communication is deemed to expedite prosecution of this application.

Respectfully submitted,

DORSEY & WHITNEY LLP

Date: October 19, 2001

By: [signature]

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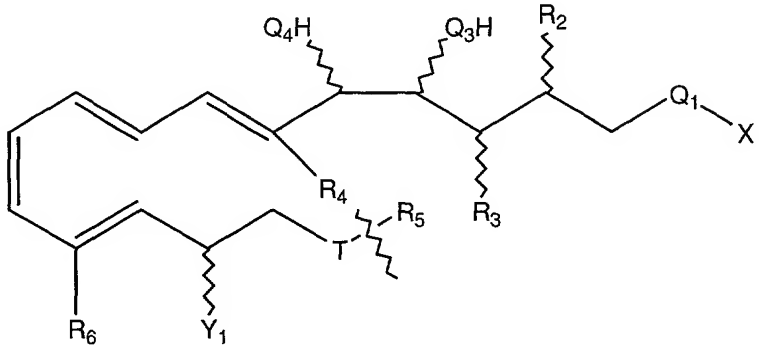
Telephone: (612) 340-8819
Facsimile: (612) 340-8856

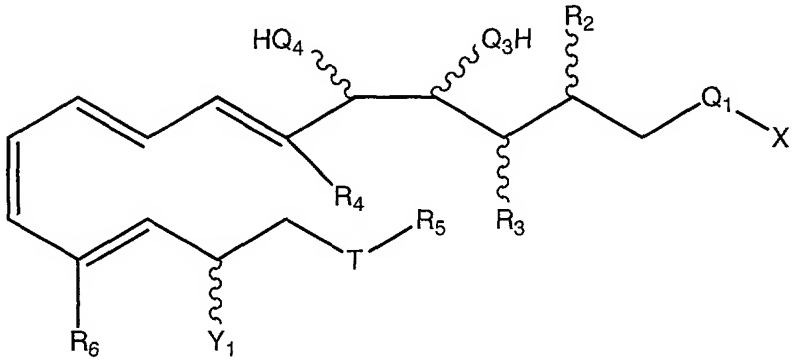
MARKED-UP VERSION SHOWING CHANGES

In the specification:

At page 11, lines 5 through 10, please delete



and insert therefore - -



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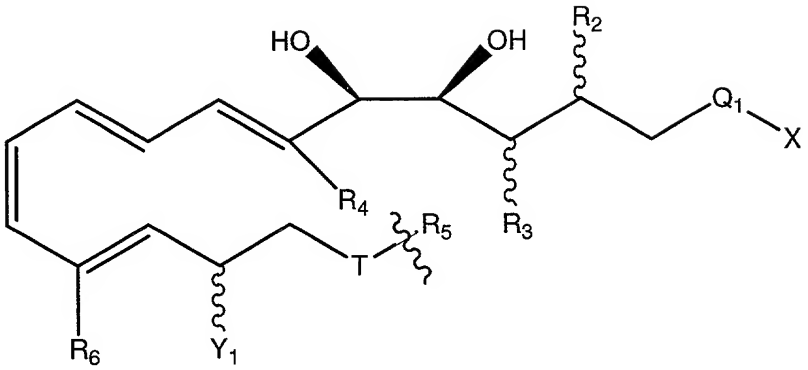
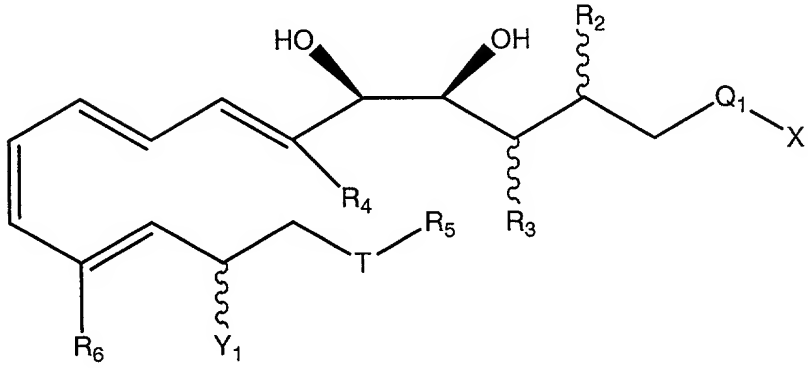
At page 14, lines 1 through 7, please delete



and insert therefore - -



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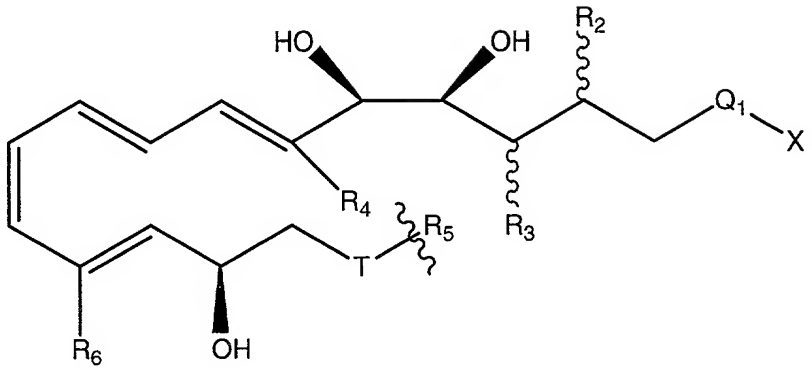
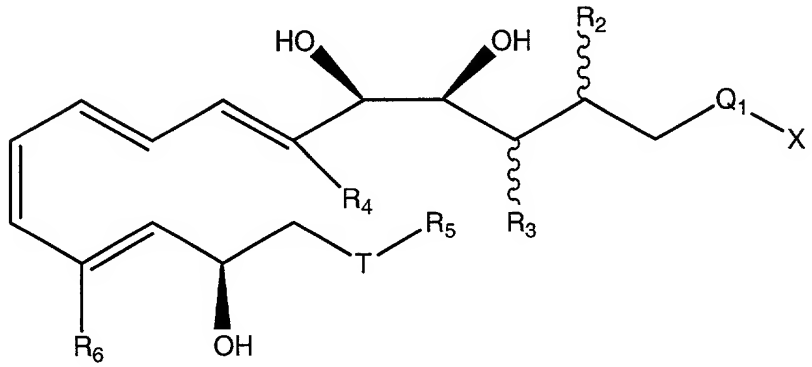
At page 17, lines 1 through 7, please delete



and insert therefore - -



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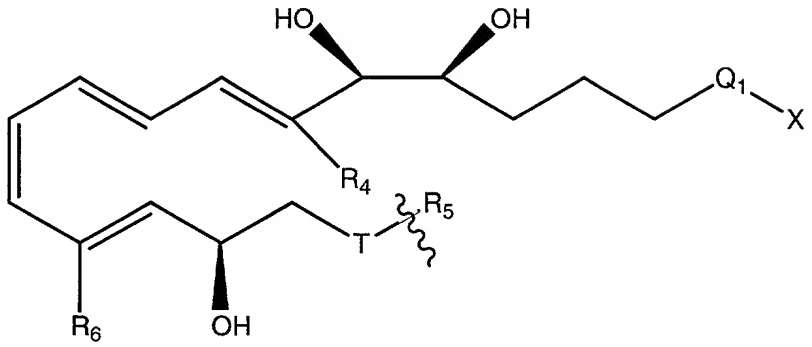
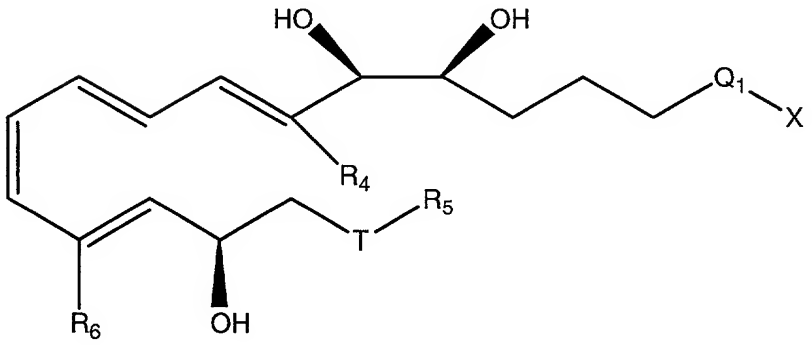
At page 19, lines 21 through 30, please delete



and insert therefore - -



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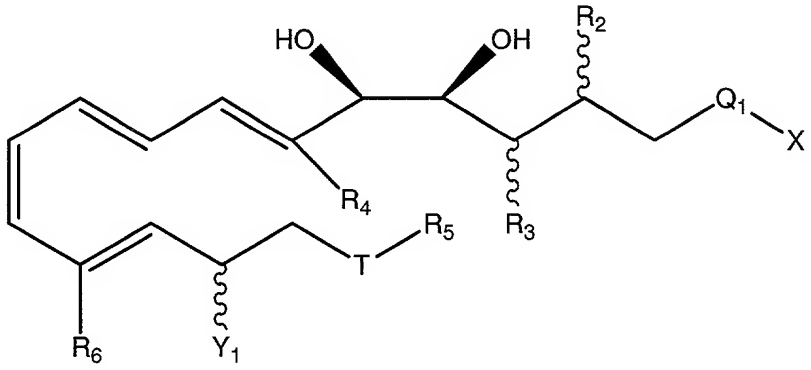
In the claims:

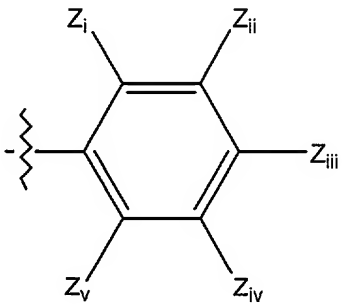
17. (New) A method for modulating a disease or condition associated with phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation in a subject, comprising

administering to the subject an effective anti-inflammatory amount of a lipoxin analog having the formula



wherein X is R_1, OR_1, or SR_1;
wherein R_1 is

(i) a hydrogen atom;
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
(iii) a cycloalkyl of 3 to 10 carbon atoms;
(iv) an aralkyl of 7 to 12 carbon atoms;
(v) phenyl;
(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or
(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

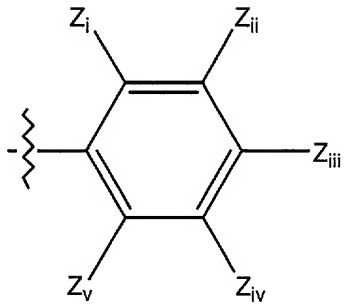
wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;
(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or
(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;
(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

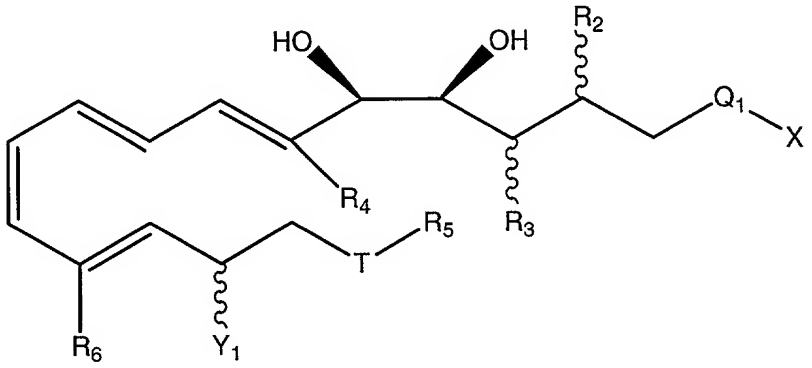
wherein T is O or S, and pharmaceutically acceptable salts thereof, such that a disease or condition associated with PLD initiated polymorphoneutrophil (PMN) inflammation in a subject is modulated.

18. (New) The method of claim 17, wherein said method is performed *in vitro*.

19. (New) The method of claim 17, wherein said method is performed *in vivo*.

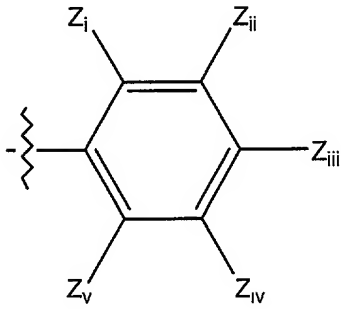
20. (New) A method for treating phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation in a subject, comprising

administering to the subject an effective anti-inflammatory amount of a lipoxin analog having the formula



wherein X is R_1, OR_1, or SR_1;
wherein R_1 is

(i) a hydrogen atom;
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
(iii) a cycloalkyl of 3 to 10 carbon atoms;
(iv) an aralkyl of 7 to 12 carbon atoms;
(v) phenyl;
(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or
(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

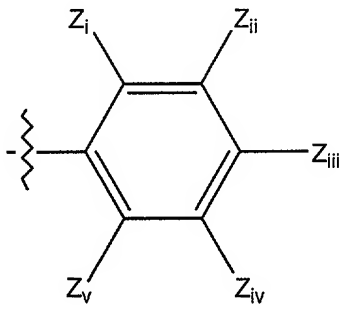
(a) H;
(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;
(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $–NO_2$, –CN, $–C(=O)–R_1$, $–SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

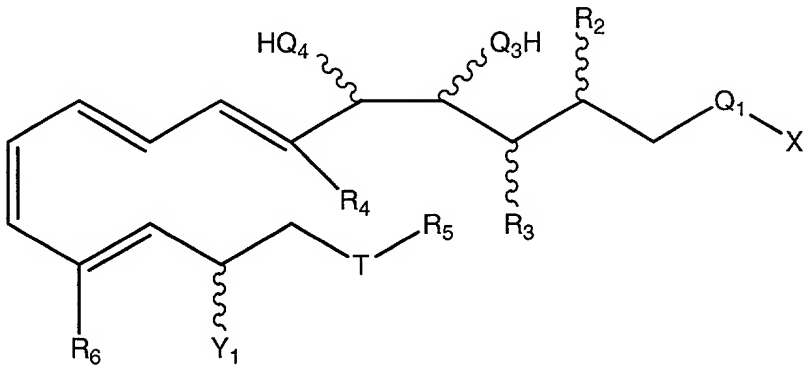
(a) H;
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein T is O or S, and pharmaceutically acceptable salts thereof, such that PLD initiated polymorphoneutrophil (PMN) inflammation is treated in a subject.

21. (New) The method of claim 20, wherein said method is performed *in vitro*.

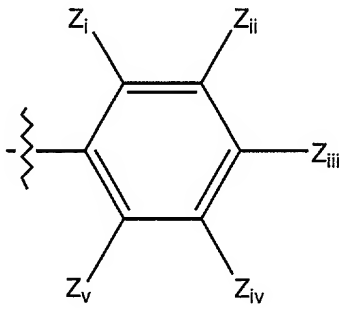
22. (New) The method of claim 20, wherein said method is performed *in vivo*.

23. (New) A method for modulating a disease or condition associated with phospholipase D (PLD) initiated superoxide generation or degranulation activity in a subject, comprising administering to the subject an effective anti-PLD amount of a lipoxin analog having the formula



wherein X is R_1, OR_1, or SR_1;
wherein R_1 is

(i) a hydrogen atom;
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
(iii) a cycloalkyl of 3 to 10 carbon atoms;
(iv) an aralkyl of 7 to 12 carbon atoms;
(v) phenyl;
(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or
(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

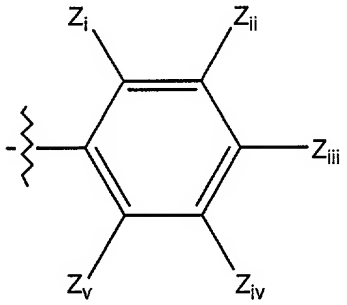
wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;
(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or
(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;
(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

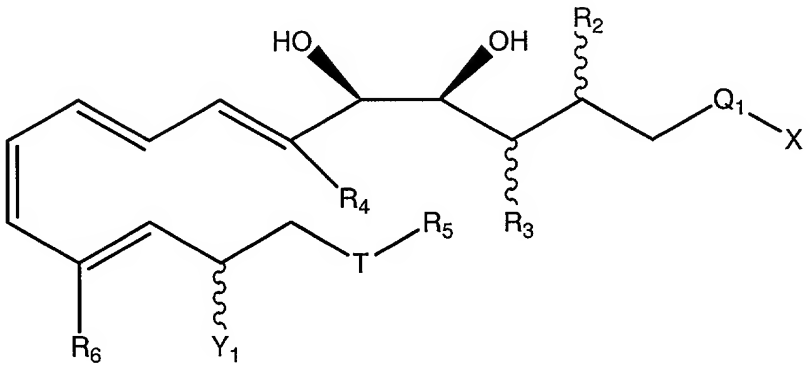
(a) H;
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein T is O or S, and pharmaceutically acceptable salts thereof, such that a disease or condition associated with PLD initiated superoxide generation or degranulation activity in a subject is modulated.

24. (New) The method of claim 23, wherein said method is performed *in vitro*.

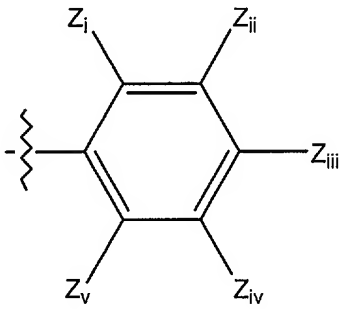
25. (New) The method of claim 23, wherein said method is performed *in vivo*.

26. (New) A method for treating phospholipase D (PLD) initiated superoxide generation or degranulation in a subject, comprising administering to the subject an effective anti-PLD amount of a lipoxin analog having the formula



wherein X is R_1, OR_1, or SR_1;
wherein R_1 is

(i) a hydrogen atom;
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
(iii) a cycloalkyl of 3 to 10 carbon atoms;
(iv) an aralkyl of 7 to 12 carbon atoms;
(v) phenyl;
(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or
(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

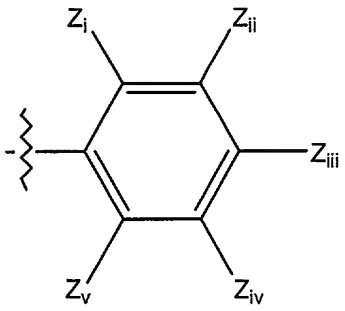
(a) H;
(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;
(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $–NO_2$, –CN, $–C(=O)–R_1$, $–SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

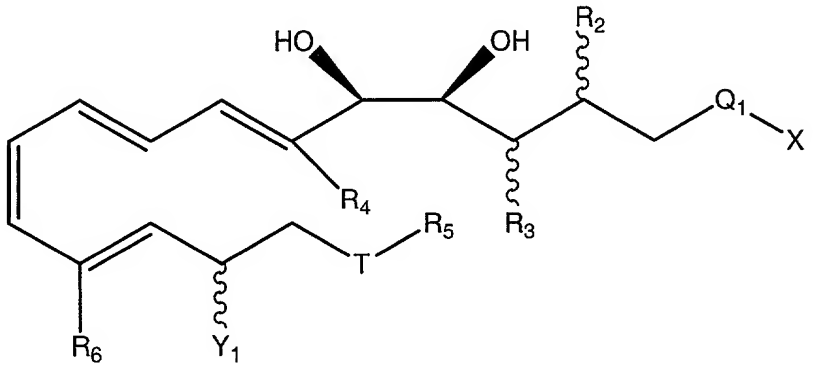
wherein T is O or S, and pharmaceutically acceptable salts thereof, such that PLD initiated superoxide generation or granulation is treated in a subject.

27. (New) The method of claim 26, wherein said method is performed *in vitro*.

28. (New) The method of claim 26, wherein said method is performed *in vivo*.

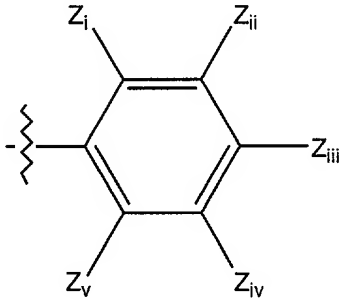
29. (New) A packaged pharmaceutical composition for treating a disease or condition associated with phospholipase D (PLD) initiated activity in a subject, comprising:

a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R_1, OR_1, or SR_1;
wherein R_1 is

(i) a hydrogen atom;
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
(iii) a cycloalkyl of 3 to 10 carbon atoms;
(iv) an aralkyl of 7 to 12 carbon atoms;
(v) phenyl;
(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or
(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

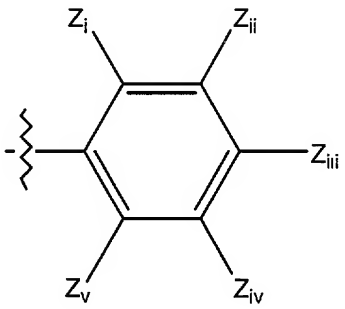
wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;
(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or
(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;
(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

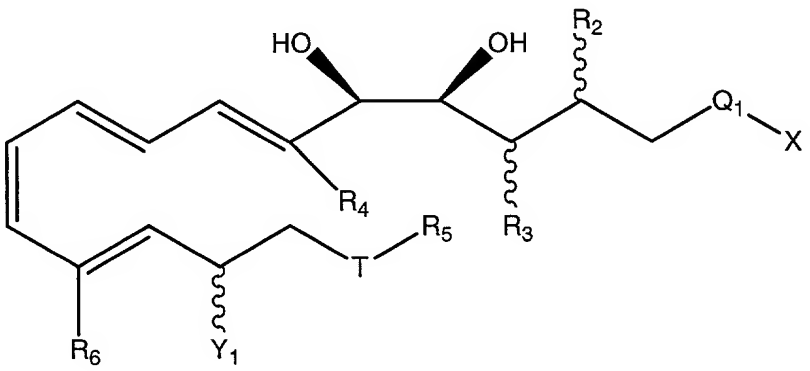
(a) H;
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein T is O or S, and pharmaceutically acceptable salts thereof; and

instructions for using said lipoxin compound for treating a disease or condition associated with PLD initiated activity in the subject.

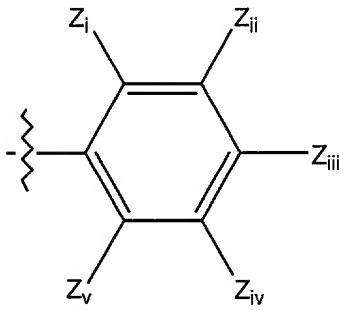
30. (New) A packaged pharmaceutical composition for treating phospholipase D initiated activity in a subject, comprising:

a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R_1, OR_1, or SR_1;
wherein R_1 is

(i) a hydrogen atom;
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
(iii) a cycloalkyl of 3 to 10 carbon atoms;
(iv) an aralkyl of 7 to 12 carbon atoms;
(v) phenyl;
(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, –CN, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or
(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

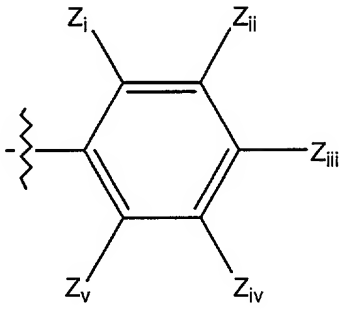
(a) H;
(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;
(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $–NO_2$, –CN, $–C(=O)–R_1$, $–SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

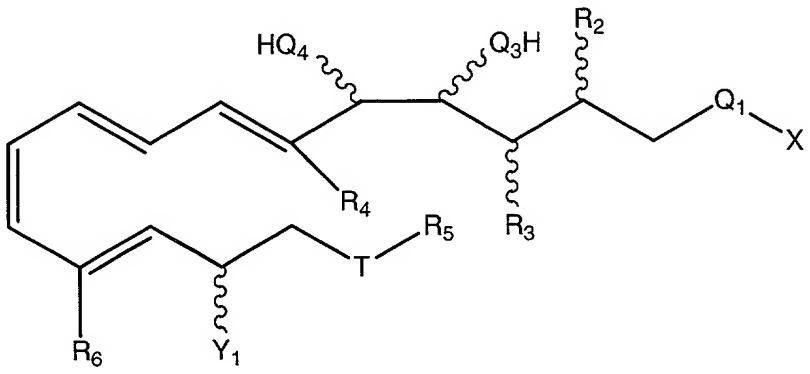
wherein R_6 is

(a) H;
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein T is O or S, and pharmaceutically acceptable salts thereof; and
instructions for using said lipoxin compound for treating PLD initiated activity in the subject.

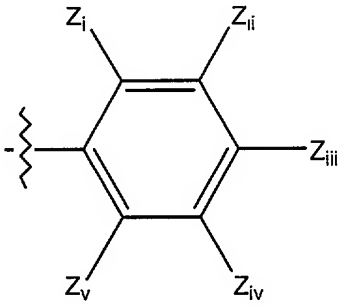
31. (New) A packaged pharmaceutical composition for treating a disease or condition associated with phospholipase D (PLD) initiated superoxide generation or degranulation activity in a subject, comprising:

a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R_1, OR_1, or SR_1;
wherein R_1 is

(i) a hydrogen atom;
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
(iii) a cycloalkyl of 3 to 10 carbon atoms;
(iv) an aralkyl of 7 to 12 carbon atoms;
(v) phenyl;
(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or
(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

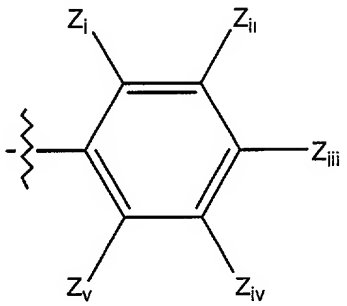
wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

(a) H;
(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or
(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;
(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, $-CN$, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

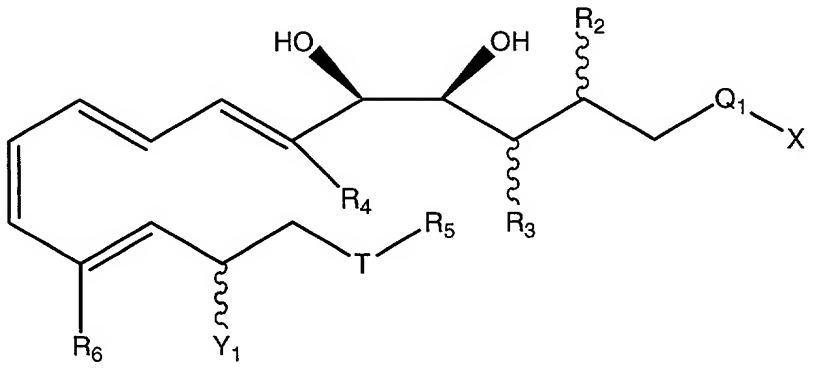
(a) H;
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein T is O or S, and pharmaceutically acceptable salts thereof; and

instructions for using said lipoxin compound for treating a disease or condition associated with PLD initiated superoxide generation or degranulation activity in the subject.

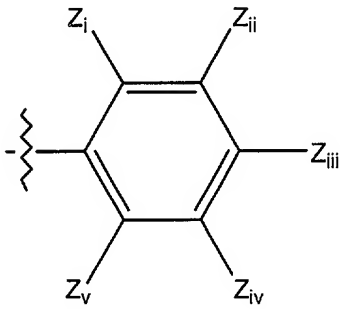
32. (New) A packaged pharmaceutical composition for treating phospholipase D (PLD) initiated superoxide generation or degranulation activity in a subject, comprising:

a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R_1, OR_1, or SR_1;
wherein R_1 is

(i) a hydrogen atom;
(ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
(iii) a cycloalkyl of 3 to 10 carbon atoms;
(iv) an aralkyl of 7 to 12 carbon atoms;
(v) phenyl;
(vi) substituted phenyl



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $-NO_2$, –CN, $-C(=O)-R_1$, $-SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

(vii) a detectable label molecule; or
(viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q_1 is (C=O), SO_2 or (CN), provided when Q_1 is CN, then X is absent;
wherein Q_3 and Q_4 are each independently O, S or NH;
wherein one of R_2 and R_3 is a hydrogen atom and the other is

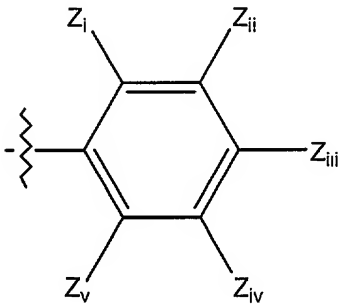
(a) H;
(b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
(c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
(d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

(e) $R_aQ_2R_b$ wherein Q_2 is –O– or –S–; wherein R_a is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein R_b is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when R_b is 0, then R_b is a hydrogen atom;

wherein R_4 is

(a) H;
(b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein R_5 is



wherein Z_i, Z_{ii}, Z_{iii}, Z_{iv} and Z_v are each independently selected from $–NO_2$, –CN, $–C(=O)–R_1$, $–SO_3H$, a hydrogen atom, halogen, methyl, $-OR_x$, wherein R_x is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein Y_1 is -OH, methyl, -SH, an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or CH_aZ_b where a+b=3, a=0 to 3, b=0 to 3 and Z is cyano, nitro or a halogen;

wherein R_6 is

(a) H;
(b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein T is O or S, and pharmaceutically acceptable salts thereof; and

instructions for using said lipoxin compound for treating PLD initiated superoxide generation or degranulation activity in the subject.